```
     FILE 'HCAPLUS' ENTERED AT 12:31:11 ON 12 AUG 2001

     FILE 'REGISTRY' ENTERED AT 12:31:13 ON 12 AUG 2001
L115          79 S L8 NOT L16,L50
L116          77 S L115 NOT (PMS/CI OR C17H18N2O6)

     FILE 'HCAPLUS' ENTERED AT 12:32:41 ON 12 AUG 2001
L117      220938 S L116
L118        7454 S L117 AND L67
L119        7454 S L118 AND L21-L25
L120          24 S L119 AND L50 (L) THU/RL
L121           4 S L120 AND L29
L122           9 S L107,L20,L121
L123           4 S L120,L114 AND L122
L124          22 S L120,L114 NOT L122
L125           3 S L124 AND (SYNERG? OR COMBINED TREATMENT)
L126           9 S L122,L123
L127           9 S L126 AND L1-L6,L19-L35,L51-L56,L60-L114,L117-L125
L128           9 S L127 AND L19
L129           5 S L127 AND L50
L130           5 S L127 AND L33
L131           5 S L129,L130
L132           4 S L128 NOT L131
L133           9 S L131,L132

     FILE 'REGISTRY' ENTERED AT 12:40:26 ON 12 AUG 2001

     FILE 'HCAPLUS' ENTERED AT 12:41:08 ON 12 AUG 2001

     FILE 'WPIX' ENTERED AT 12:41:23 ON 12 AUG 2001
                E AOMATSU A/AU
L134            2 S E3
                E A61K031-195/IC,ICM,ICS
L135         3157 S E3-E5
L136           76 S A61P025/IC,ICM,ICS,ICA,ICI AND L135
L137            2 S L136 AND AMINO (S) BUTANOIC
L138           13 S L135 AND AMINO (S) BUTANOIC
L139            1 S L135 AND AMINO (S) BUTANOATE
L140           14 S L137-L139
L141            7 S L140 AND 4 AMINO 3
L142            7 S L134,L141
L143            6 S L135 AND 4 AMINOBUTYRIC
L144            1 S L135 AND 4 AMINOBUTANO?
L145            6 S L143,L144
L146           12 S L142,L145
L147            3 S L135 AND 4 AMINO BUT?
L148           13 S L146,L147
L149            3 S M782/M0,M1,M2,M3,M4,M5,M6 AND L148
L150          120 S L33
L151            3 S L148 AND L150
L152            5 S L149,L151
                E GABAPENTIN/DCN
                E E3+ALL
L153           53 S E2
                E PREGABALIN/DCN
                E BACLOFEN/DCN
                E E4+ALL
L154           29 S E2
L155            2 S BACLOPHEN?
L156            2 S L153-L155 AND L148
L157            5 S L152,L156

     FILE 'WPIX' ENTERED AT 12:57:53 ON 12 AUG 2001
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L57           7 S L36 NOT L50
L58           1 S L57 AND C4H9NO2
L59           6 S L57 NOT L58

     FILE 'HCAPLUS' ENTERED AT 11:53:39 ON 12 AUG 2001
L60           5 S L59
L61           4 S L59 AND L32
L62           1 S L60 NOT L61
L63          15 S L56,L61
L64         389 S L58/D
L65           7 S L64 AND L32
L66          35 S L32,L63,L65
L67       21856 S L19,L51,L64 AND (PD<=19980515 OR PRD<=19980518 OR AD<=1998051
L68         421 S L16 (L) THU/RL AND L67
L69         187 S L68 AND L21-L25
L70          20 S L68 AND L26
L71          18 S L68 AND L28
L72          25 S L70,L71
L73          10 S L72 AND L33,L51
L74           7 S L72 AND L63
L75           3 S L73 NOT L74
L76         623 S L67 AND (STABLE OR UNSTABLE OR STABIL? OR INSTABIL?)
L77           4 S L76 AND L66
                E STAB/CT
                E E12+ALL
L78        4819 S E3
                E E25+ALL
L79       72624 S E2+NT
                E E22+ALL
L80       66439 S E2+NT
                E E17+ALL
L81        8534 S E1+NT
L82         253 S E14+NT
L83        5598 S E17+NT
L84          54 S L67 AND L78-L83
L85          19 S L84 AND AMINO ACID?/CT
L86          48 S L84 AND L21-L26
L87          13 S L84 AND L28
L88           3 S L84 AND L31
L89           8 S L84 AND L33
L90           8 S L84 AND L51
L91          49 S  L85-L90
L92           3 S L91 AND L72
L93           1 S L92 AND L64
L94          93 S L20,L32,L66,L72-L75,L77,L91-L93
L95          20 S L94 AND 63/SC
L96          46 S L94 AND (COMPOSITION OR COMBIN? OR MIX? OR SYNERG? OR CONCOMI
L97          34 S L96 AND (1 OR 63)/SC,SX
L98          29 S L96 AND THU/RL
L99          36 S L97,L98
L100         16 S L94 AND (?COMPLEX? OR ?CONJUGAT?)
L101         41 S L99,L100
L102         30 S L101 AND AMINO ACID?/CT
L103         11 S L101 NOT L102
L104          8 S L102 AND STAB?
L105         22 S L102 NOT L104
L106          7 S L105 AND (MODIFIED OR AGONIST OR IMPROVED OR TOPICAL OR SUGAR
                SEL DN 6 7
L107          5 S L106 NOT E1-E2
L108       1774 S L51 AND L67
L109        263 S L108 AND L68
L110        263 S L50 (L) THU/RL AND L109
L111          6 S L26 AND L110
L112          6 S L29 AND L110
L113          6 S L111,L112
L114          6 S L113 AND L21-L25
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     FILE 'REGISTRY' ENTERED AT 11:24:49 ON 12 AUG 2001
L7          104 S E1-E104
L8           89 S L7 AND N/ELS
L9              STR
L10           2 S L9
L11             SCR 1568 AND 1312
L12           4 S L9 AND L11
L13             SCR 1007
L14           2 S L9 AND L11 AND L13
L15           2 S L12 NOT L14
L16        1165 S L9 AND L11 FUL
                SAV L16 KWON674/A
L17          10 S L7 AND L16
L18          94 S L7 NOT L17

     FILE 'HCAPLUS' ENTERED AT 11:31:47 ON 12 AUG 2001
L19       24235 S L16
L20           3 S L6 AND L19
                E AMINO ACID/CT
                E E61+NT
L21       22136 S E1-E50 AND L19
L22        1322 S E51-E100 AND L19
L23        8324 S E101-E150 AND L19
L24        2958 S E151-E200 AND L19
L25         292 S E201-E222 AND L19
                E AMINO ACIDS/CT
L26        2066 S AMINO ACIDS/CT (L) THU/RL
L27          49 S L26 AND L21-L25
                E AMINO ACIDS, BIOLOGICAL STUDIES/CT
L28        3298 S E3 AND L19
L29          30 S E3(L)THU/RL AND L19
L30          49 S L27,L29
L31          49 S L21-L29 AND L30
L32          35 S L31 AND (1 OR 63)/SC,SX
L33        3505 S GABAPENTIN? OR PREGABALIN? OR BACLOFEN?
L34           0 S 3()(AMINOMETHYL OR AMINO METHYL)()4()(CYCLOHEXYL OR CYCLO HEX
L35           0 S 3()(AMINOMETHYL OR AMINO METHYL)()4()(CYCLOHEXYLBUTANOIC OR C
                SEL HIT RN L20

     FILE 'REGISTRY' ENTERED AT 11:45:32 ON 12 AUG 2001
L36          10 S E1-E10
L37           3 S 1134-47-0 OR 60142-96-3 OR 148553-50-8
L38           7 S L36 NOT L37
L39           6 S L38 AND C6/ES
L40           3 S L39 AND 46.150.1/RID
L41           3 S L39 NOT L40
L42           6 S C8H17NO2/MF AND L16
L43           3 S L42 AND HEXANOIC AND 5
L44           5 S L37,L43
L45          12 S L16 AND C10H12CLNO2/MF
L46           9 S L45 AND BENZENEPROPANOIC AND 4 CHLORO
L47           3 S L46 NOT (11C# OR 13C# OR 14C# OR LABELED OR (D OR T)/ELS)
L48          34 S L16 AND C9H17NO2/MF
L49           2 S L48 AND 46.150.1/RID
L50           7 S L37,L44,L47

     FILE 'HCAPLUS' ENTERED AT 11:51:48 ON 12 AUG 2001
L51        2191 S L50
L52          13 S L51 AND L32
L53          13 S L33 AND L32
L54          14 S L52,L53
L55           3 S L20 AND L51,L32,L33
L56          14 S L54,L55

     FILE 'REGISTRY' ENTERED AT 11:52:57 ON 12 AUG 2001
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=> fil reg
FILE 'REGISTRY' ENTERED AT 12:40:26 ON 12 AUG 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

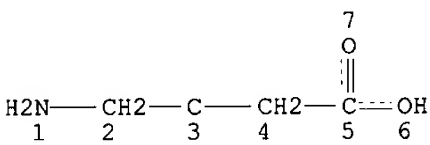
STRUCTURE FILE UPDATES: 10 AUG 2001 HIGHEST RN 351153-64-5
DICTIONARY FILE UPDATES: 10 AUG 2001 HIGHEST RN 351153-64-5

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d sta que l16
L9 STR



1. Gabapentin / pregabalin

NODE ATTRIBUTES:
NSPEC IS RC AT 3
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 7

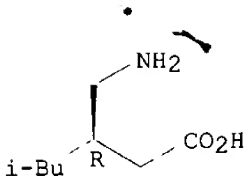
STEREO ATTRIBUTES: NONE
L11 SCR 1568 AND 1312
L16 1165 SEA FILE=REGISTRY SSS FUL L9 AND L11

100.0% PROCESSED 238676 ITERATIONS 1165 ANSWERS
SEARCH TIME: 00.00.09

=> d ide can tot l50

L50 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 148553-51-9 REGISTRY
CN **Hexanoic acid, 3-(aminomethyl)-5-methyl-, (3R)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Hexanoic acid, 3-(aminomethyl)-5-methyl-, (R)-**
OTHER NAMES:
CN (R)-Pregabalin
CN PD 144550
FS STEREOSEARCH
MF **C8 H17 N O2**
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, DRUGUPDATES, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



13 REFERENCES IN FILE CA (1967 TO DATE)
13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:320768

REFERENCE 2: 134:125863

REFERENCE 3: 132:274197

REFERENCE 4: 132:102843

REFERENCE 5: 131:97392

REFERENCE 6: 130:191891

REFERENCE 7: 130:191890

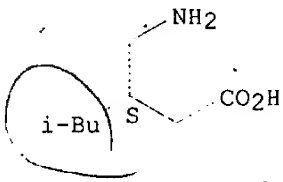
REFERENCE 8: 130:90504

REFERENCE 9: 129:156883

REFERENCE 10: 129:62851

L50 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN **148553-50-8** REGISTRY
CN **Hexanoic acid, 3-(aminomethyl)-5-methyl-, (3S)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Hexanoic acid, 3-(aminomethyl)-5-methyl-, (S)-**
OTHER NAMES:
CN CI 1008
CN PD 144723
CN Pregabalin
FS STEREOSEARCH
MF **C8 H17 N O2**
CI COM
SR CA
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



61 REFERENCES IN FILE CA (1967 TO DATE)
62 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:101698

REFERENCE 2: 135:66248

REFERENCE 3: 135:24671

REFERENCE 4: 134:331617

REFERENCE 5: 134:320768

REFERENCE 6: 134:285590

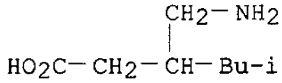
REFERENCE 7: 134:271290

REFERENCE 8: 134:202706

REFERENCE 9: 134:198075

REFERENCE 10: 134:131540

L50 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 128013-69-4 REGISTRY
CN **Hexanoic acid, 3-(aminomethyl)-5-methyl- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
DR 130912-52-6
MF **C8 H17 N O2**
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, DRUGUPDATES, SYNTHLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:288785

REFERENCE 2: 131:58836

REFERENCE 3: 130:38664

REFERENCE 4: 128:149590

REFERENCE 5: 126:104423

REFERENCE 6: 126:103837

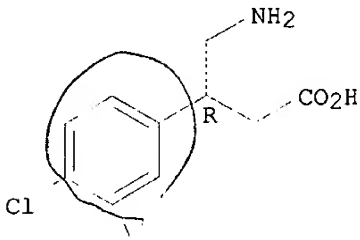
REFERENCE 7: 118:182788

REFERENCE 8: 113:41285

L50 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 69308-37-8 REGISTRY
CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (.beta.R)-(9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (R)-**
OTHER NAMES:
CN (-)-Baclofen
CN (R)-(-)-Baclofen
CN **(R)-4-Amino-3-(4-chlorophenyl)butanoic acid**
CN (R)-Baclofen
CN D-Baclofen
CN l-Baclofen
CN R-(-)-Baclofen

FS STEREOSEARCH
MF **C10 H12 Cl N O2**
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CHEMCATS, PROMT, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



187 REFERENCES IN FILE CA (1967 TO DATE)
187 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:306509

REFERENCE 2: 134:231440

REFERENCE 3: 134:142141

REFERENCE 4: 134:141758

REFERENCE 5: 133:329945

REFERENCE 6: 133:305526

REFERENCE 7: 133:183136

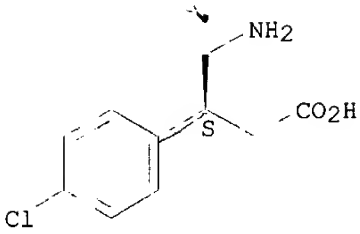
REFERENCE 8: 133:177033

REFERENCE 9: 133:172447

REFERENCE 10: 132:202993

L50 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 66514-99-6 REGISTRY
CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (.beta.S)-(9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (S)-**
OTHER NAMES:
CN (+)-Baclofen
CN **(S)-4-Amino-3-(4-chlorophenyl)butanoic acid**
CN (S)-Baclofen
CN d-Baclofen
CN L-(+)-Baclofen
CN L-Baclofen
CN S(+)-Baclofen
FS STEREOSEARCH
MF **C10 H12 Cl N O2**
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



222 REFERENCES IN FILE CA (1967 TO DATE)
222 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:290661

REFERENCE 2: 134:231440

REFERENCE 3: 133:217711

REFERENCE 4: 133:183136

REFERENCE 5: 131:299661

REFERENCE 6: 131:284829

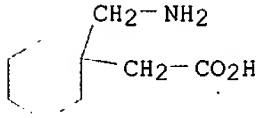
REFERENCE 7: 131:252676

REFERENCE 8: 131:237936

REFERENCE 9: 131:157932

REFERENCE 10: 131:139952

L50 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN **60142-96-3** REGISTRY
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-(Aminomethyl)cyclohexaneacetic acid
CN CI 945
CN Gabapentin
CN Go 3450
CN GOE 2450
CN Neurontin
FS 3D CONCORD
MF C9 H17 N O2
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



447 REFERENCES IN FILE CA (1967 TO DATE)

18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
151 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:111992

REFERENCE 2: 135:105918

REFERENCE 3: 135:102395

REFERENCE 4: 135:102372

REFERENCE 5: 135:101700

REFERENCE 6: 135:97445

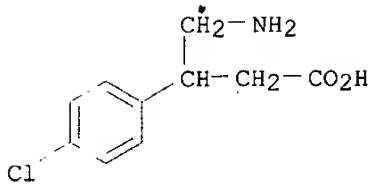
REFERENCE 7: 135:87387

REFERENCE 8: 135:87084

REFERENCE 9: 135:87018

REFERENCE 10: 135:86988

L50 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN **1134-47-0** REGISTRY
CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydrocinnamic acid, .beta.-(aminomethyl)-p-chloro- (7CI, 8CI)
OTHER NAMES:
CN (.+-.)-Baclofen
CN **.beta.-(4-Chlorophenyl)-.gamma.-aminobutyric acid**
CN .beta.-(Aminomethyl)-p-chlorohydrocinnamic acid
CN .beta.-(p-Chlorophenyl)-.gamma.-aminobutyric acid
CN .beta.-p-Chlorophenyl-GABA
CN **4-Amino-3-(4-chlorophenyl)butyric acid**
CN 4-Amino-3-(p-chlorophenyl)butyric acid
CN Ba 34647
CN Baclofen
CN C 34647Ba
CN CIBA Ba 34647
CN DL-4-Amino-3-p-chlorophenylbutanoic acid
CN DL-Baclofen
CN dl-Baclofen
CN Lioresal
FS 3D CONCORD
DR 62594-36-9
MF **C10 H12 Cl N O2**
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



1364 REFERENCES IN FILE CA (1967 TO DATE)
36 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1366 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:111958

REFERENCE 2: 135:102802

REFERENCE 3: 135:102657

REFERENCE 4: 135:55467

REFERENCE 5: 135:44168

REFERENCE 6: 135:41034

REFERENCE 7: 135:29335

REFERENCE 8: 135:28954

REFERENCE 9: 135:24671

REFERENCE 10: 135:17656

=> d his

(FILE 'HOME' ENTERED AT 11:22:43 ON 12 AUG 2001)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:22:57 ON 12 AUG 2001
E WO9959573/PN
L1 1 S E3
E WO99-US10190/AP,PRN
L2 1 S E3,E4
E JP98-133113/AP,PRN
L3 1 S E4
L4 1 S L1-L3
E AOMATSU A/AU
L5 4 S E4
L6 4 S L4,L5
SEL RN

FILE 'REGISTRY' ENTERED AT 11:24:49 ON 12 AUG 2001
L7 104 S E1-E104
L8 89 S L7 AND N/ELS
L9 STR
L10 2 S L9
L11 SCR 1568 AND 1312
L12 4 S L9 AND L11
L13 SCR 1007
L14 2 S L9 AND L11 AND L13
L15 2 S L12 NOT L14
L16 1165 S L9 AND L11 FUL
SAV L16 KWON674/A

```
L17          10 S L7 AND L16
L18          94 S L7 NOT L17

     FILE 'HCAPLUS' ENTERED AT 11:31:47 ON 12 AUG 2001
L19       24235 S L16
L20           3 S L6 AND L19
                E AMINO ACID/CT
                E E61+NT
L21       22136 S E1-E50 AND L19
L22        1322 S E51-E100 AND L19
L23        8324 S E101-E150 AND L19
L24        2958 S E151-E200 AND L19
L25         292 S E201-E222 AND L19
                E AMINO ACIDS/CT
L26        2066 S AMINO ACIDS/CT (L) THU/RL
L27          49 S L26 AND L21-L25
                E AMINO ACIDS, BIOLOGICAL STUDIES/CT
L28        3298 S E3 AND L19
L29          30 S E3(L)THU/RL AND L19
L30          49 S L27,L29
L31          49 S L21-L29 AND L30
L32          35 S L31 AND (1 OR 63)/SC,SX
L33        3505 S GABAPENTIN? OR PREGABALIN? OR BACLOFEN?
L34           0 S 3()(AMINOMETHYL OR AMINO METHYL)()4()(CYCLOHEXYL OR CYCLO HEX
L35           0 S 3()(AMINOMETHYL OR AMINO METHYL)()4()(CYCLOHEXYLBUTANOIC OR C
                SEL HIT RN L20

     FILE 'REGISTRY' ENTERED AT 11:45:32 ON 12 AUG 2001
L36          10 S E1-E10
L37           3 S 1134-47-0 OR 60142-96-3 OR 148553-50-8
L38           7 S L36 NOT L37
L39           6 S L38 AND C6/ES
L40           3 S L39 AND 46.150.1/RID
L41           3 S L39 NOT L40
L42           6 S C8H17NO2/MF AND L16
L43           3 S L42 AND HEXANOIC AND 5
L44           5 S L37,L43
L45          12 S L16 AND C10H12CLNO2/MF
L46           9 S L45 AND BENZENEPROPANOIC AND 4 CHLORO
L47           3 S L46 NOT (11C# OR 13C# OR 14C# OR LABELED OR (D OR T)/ELS)
L48          34 S L16 AND C9H17NO2/MF
L49           2 S L48 AND 46.150.1/RID
L50           7 S L37,L44,L47

     FILE 'HCAPLUS' ENTERED AT 11:51:48 ON 12 AUG 2001
L51        2191 S L50
L52          13 S L51 AND L32
L53          13 S L33 AND L32
L54          14 S L52,L53
L55           3 S L20 AND L51,L32,L33
L56          14 S L54,L55

     FILE 'REGISTRY' ENTERED AT 11:52:57 ON 12 AUG 2001
L57           7 S L36 NOT L50
L58           1 S L57 AND C4H9NO2
L59           6 S L57 NOT L58

     FILE 'HCAPLUS' ENTERED AT 11:53:39 ON 12 AUG 2001
L60           5 S L59
L61           4 S L59 AND L32
L62           1 S L60 NOT L61
L63          15 S L56,L61
L64         389 S L58/D
L65           7 S L64 AND L32
L66          35 S L32,L63,L65
L67       21856 S L19,L51,L64 AND (PD<=19980515 OR PRD<=19980518 OR AD<=1998051
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L68          421 S L16 (L) THU/RL AND L67
L69          187 S L68 AND L21-L25
L70           20 S L68 AND L26
L71           18 S L68 AND L28
L72           25 S L70,L71
L73           10 S L72 AND L33,L51
L74            7 S L72 AND L63
L75            3 S L73 NOT L74
L76          623 S L67 AND (STABLE OR UNSTABLE OR STABIL? OR INSTABIL?)
L77            4 S L76 AND L66
                 E STAB/CT
                 E E12+ALL
L78         4819 S E3
                 E E25+ALL
L79        72624 S E2+NT
                 E E22+ALL
L80        66439 S E2+NT
                 E E17+ALL
L81         8534 S E1+NT
L82          253 S E14+NT
L83         5598 S E17+NT
L84           54 S L67 AND L78-L83
L85           19 S L84 AND AMINO ACID?/CT
L86           48 S L84 AND L21-L26
L87           13 S L84 AND L28
L88            3 S L84 AND L31
L89            8 S L84 AND L33
L90            8 S L84 AND L51
L91           49 S  L85-L90
L92            3 S L91 AND L72
L93            1 S L92 AND L64
L94           93 S L20,L32,L66,L72-L75,L77,L91-L93
L95           20 S L94 AND 63/SC
L96           46 S L94 AND (COMPOSITION OR COMBIN? OR MIX? OR SYNERG? OR CONCOMI
L97           34 S L96 AND (1 OR 63)/SC,SX
L98           29 S L96 AND THU/RL
L99           36 S L97,L98
L100          16 S L94 AND (?COMPLEX? OR ?CONJUGAT?)
L101          41 S L99,L100
L102          30 S L101 AND AMINO ACID?/CT
L103          11 S L101 NOT L102
L104           8 S L102 AND STAB?
L105          22 S L102 NOT L104
L106           7 S L105 AND (MODIFIED OR AGONIST OR IMPROVED OR TOPICAL OR SUGAR
                 SEL DN 6 7
L107           5 S L106 NOT E1-E2
L108        1774 S L51 AND L67
L109         263 S L108 AND L68
L110         263 S L50 (L) THU/RL AND L109
L111           6 S L26 AND L110
L112           6 S L29 AND L110
L113           6 S L111,L112
L114           6 S L113 AND L21-L25

     FILE 'HCAPLUS' ENTERED AT 12:31:11 ON 12 AUG 2001

     FILE 'REGISTRY' ENTERED AT 12:31:13 ON 12 AUG 2001
L115          79 S L8 NOT L16,L50
L116          77 S L115 NOT (PMS/CI OR C17H18N2O6)

     FILE 'HCAPLUS' ENTERED AT 12:32:41 ON 12 AUG 2001
L117      220938 S L116
L118        7454 S L117 AND L67
L119        7454 S L118 AND L21-L25
L120          24 S L119 AND L50 (L) THU/RL
L121           4 S L120 AND L29
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L122          9 S L107,L20,L121
L123          4 S L120,L114 AND L122
L124         22 S L120,L114 NOT L122
L125          3 S L124 AND (SYNERG? OR COMBINED TREATMENT)
L126          9 S L122,L123
L127          9 S L126 AND L1-L6,L19-L35,L51-L56,L60-L114,L117-L125
L128          9 S L127 AND L19
L129          5 S L127 AND L50
L130          5 S L127 AND L33
L131          5 S L129,L130
L132          4 S L128 NOT L131
L133          9 S L131,L132

     FILE 'REGISTRY' ENTERED AT 12:40:26 ON 12 AUG 2001

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 12:41:08 ON 12 AUG 2001
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26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1947 - 12 Aug 2001  VOL 135 ISS 8
FILE LAST UPDATED: 10 Aug 2001  (20010810/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

 This file supports REG1stRY for direct browsing and searching of
 all substance data from the REGISTRY file.  Enter HELP FIRST for
 more information.

HCAplus now provides online access to patents and literature covered
in CA from 1947 to the present.  On April 22, 2001, bibliographic
information and abstracts were added for over 2.2 million references
published in CA from 1947 to 1966.


=> d bib abs hitrn tot l133

L133 ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2001 ACS
AN   2000:608551  HCAPLUS
DN   133:213151
TI   Pharmaceutical compositions and methods for improved
     delivery of hydrophobic therapeutic agents
IN   Patel, Manesh V.; Chen, Feng-Jing
PA   Lipocine, Inc., USA
SO   PCT Int. Appl., 98 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2000050007     A1    20000831      WO 2000-US165    20000105
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
```

BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-258654 A 19990226
AB The present invention relates to triglyceride-free pharmaceutical **compns.** for delivery of hydrophobic therapeutic agents. **Compns.** of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a **combination** of a hydrophilic surfactant and a hydrophobic surfactant. Upon diln. with an aq. solvent, the **compn.** forms a clear, aq. dispersion of the surfactants contg. the therapeutic agent. The invention also provides methods of treatment with hydrophobic therapeutic agents using these **compns.** A pharmaceutical **compn.** contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacel186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.
IT **51-48-9**, L-Thyroxine, biological studies **1134-47-0**, **Baclofen 60142-96-3**, **Gabapentin**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical **compns.** and methods for improved delivery of hydrophobic therapeutic agents)
RE.CNT 4
RE
(1) Crooks; US 4572915 A 1986 HCAPLUS
(2) Muller; US 4719239 A 1988 HCAPLUS
(3) Schmidt; US 4727109 A 1988 HCAPLUS
(4) Story; US 4944949 A 1990 HCAPLUS

L133 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:80040 HCAPLUS
DN 132:127733
TI **Stabilized** solid preparations of 4-amino-3-substituted-butanoic acid derivatives and their manufacture
IN **Aomatsu, Akira**
PA Warner Lambert Co., USA
SO Jpn. Kokai Tokkyo Koho, 34 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2000034227	A2	20000202	JP 1999-133769	19990514 <--
PRAI JP 1998-133112	A	19980515 <--		

OS MARPAT 132:127733
AB Solid prepns. of H2NCH2CR1R2CH2CO2H [I; R1 = H, OH, Me, Et; R2 = various (un)substituted hydrocarbyl (definitions are described in detail)], useful as nervous system agents for treatment of epilepsy, syncope, head trauma, cerebral dysfunction, Alzheimer disease, Huntington chorea, parkinsonism, etc., are manufd. by adding water-holding agents such as ethylene glycol, propylene glycol, glycerin, etc., and optionally excipients. The prepns. may addnl. contain neutral amino acids. Water-holding agents prevents deterioration of I due to lactam formation. **Gabapentin** was spray-coated with an aq. propylene glycol soln. to give powder contg. 0.003% lactam. The powder was stored in a sealed container at 60 degree. for 2 wk to show lactam content 0.011%, vs. 0.017% for control powder contg. no propylene glycol.
IT **56-40-6**, Glycine, biological studies **56-41-7**, L-Alanine, biological studies **61-90-5**, L-Leucine, biological studies **72-18-4**, L-Valine, biological studies **73-32-5**, L-Isoleucine, biological studies **302-72-7**, Alanine **319-78-8**, D-Isoleucine **328-38-1**, D-Leucine **328-39-2**, Leucine **338-69-2**, D-Alanine **443-79-8**, Isoleucine **516-06-3**, Valine **640-68-6**, D-Valine
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**stabilization** of solid prepns. of 4-amino-3-substituted-butanoic acid derivs. as nervous system agents by addn. of water-holding agents)

IT **1134-47-0, Baclofen 30200-05-6**
60142-96-3, Gabapentin 148553-50-8,
Pregabalin 206749-40-8 256418-06-1
256418-07-2
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**stabilization** of solid prepns. of 4-amino-3-substituted-butanoic acid derivs. as nervous system agents by addn. of water-holding agents)

L133 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:753061 HCAPLUS
DN 132:6349
TI Preparation of **stabilized** pharmaceuticals containing .gamma.-aminobutyric acid derivatives
IN **Aomatsu, Akira**
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9959573	A1	19991125	WO 1999-US10190	19990510	<--
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	AU 9940735	A1	19991206	AU 1999-40735	19990510	<--
	BR 9910508	A	20010102	BR 1999-10508	19990510	<--
	EP 1077692	A1	20010228	EP 1999-924166	19990510	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	NO 2000005768	A	20001114	NO 2000-5768	20001114	<--
PRAI	JP 1998-133113	A	19980515	<--		
	WO 1999-US10190	W	19990510	<--		

OS MARPAT 132:6349
AB The present invention provides a **stabilized** pharmaceutical prepn. of a 4-amino-3-substituted butanoic acid deriv. which can be obtained by incorporating an amino acid as a **stabilizer**. Thus, a sample was prepd. by dissolving 500 mg of **gabapentin** crystals in water to make up a total vol. of 10 mL and stored under various conditions. The degrdn. of **gabapentin** stored, e.g., for 4 wk at 45.degree. was prevented by the addn. of L-valine or glycine.
IT **51-48-9**, L-Thyroxine, biological studies **56-12-2D**, .gamma.-Aminobutyric acid, derivs. **56-40-6**, Glycine, biological studies **56-41-7**, L-Alanine, biological studies **56-45-1**, L-Serine, biological studies **56-84-8**, L-Aspartic acid, biological studies **56-86-0**, L-Glutamic acid, biological studies **56-87-1**, L-Lysine, biological studies **56-89-3**, L-Cystine, biological studies **59-92-7**, Levodopa, biological studies **60-18-4**, L-Tyrosine, biological studies **61-90-5**, L-Leucine, biological studies **61-90-5D**, L-Leucine, hydroxy derivs. **62-57-7**, 2-Aminoisobutyric acid **63-68-3**, L-Methionine, biological studies **63-91-2**, L-Phenylalanine, biological studies **70-26-8**, L-Ornithine **72-18-4**, L-Valine, biological studies **72-19-5**, L-Threonine, biological studies **73-22-3**, L-Tryptophan, biological studies **73-22-3D**, L-Tryptophan, hydroxy or Me derivs. **73-32-5**, L-IsoLeucine, biological studies **73-32-5D**, L-Isoleucine, hydroxy

derivs. **74-79-3**, L-Arginine, biological studies **156-86-5**
, L-HomoArginine **300-38-9**, 3,5-DiBromo-L-Tyrosine
300-39-0, 3,5-Diiodo-L-Tyrosine **302-72-7**, Alanine
327-57-1, L-NorLeucine **372-75-8**, Citrulline
496-93-5, L-Canaline **537-49-5**, N-Methyl-L-Tyrosine
537-55-3, N-Acetyl-L-Tyrosine **543-38-4**, L-Canavanine
555-30-6, L-Methyldopa **587-33-7 595-40-4**,
L-IsoValine **626-72-2**, L-HomoCystine **638-23-3**
672-15-1, L-HomoSerine **921-52-8**, Diaminosuccinic acid
1115-93-1, S-Propyl-L-Cysteine **1118-90-7**
1118-90-7D, hydroxy derivs. **1134-47-0**, **Baclofen**
1187-84-4, S-Methyl-L-Cysteine **1190-94-9**,
Hydroxy-L-lysine **1492-24-6**, L-2-Aminobutyric acid
1492-24-6D, L-2-Aminobutyric acid, derivs. **2835-06-5**
2835-06-5D, hydroxy derivs. **4033-39-0**,
L-2,3-Diaminopropionic acid **6152-89-2 6600-40-4**,
L-NorValine **6600-40-4D**, L-Norvaline, derivs. **6665-12-9**
7423-93-0, 3-Chloro-L-Tyrosine **7540-67-2**,
O-Acetyl-L-Homoserine **13073-35-3**, L-Ethionine **15091-76-6**
, N-Hydroxy-L-Alanine **16055-12-2 16354-58-8**,
N-Acetyl-L-Serine **16804-57-2 17093-74-2**,
N-Acetyl-L-Threonine **17268-93-8 17673-71-1**,
O-Butyl-L-HomoSerine **18312-28-2**, O-Propyl-L-HomoSerine
21593-77-1, S-Allyl-L-Cysteine **25148-30-5**,
L-HomoMethionine **26630-55-7 26630-55-7D**, hydroxy
derivs. **26911-39-7 29784-96-1 30200-05-6**
35187-58-7 38739-13-8, 3-Bromo-L-Tyrosine
44902-02-5 60142-96-3, **Gabapentin**
71292-20-1 116783-26-7 148553-50-8,
Pregabalin 187611-96-7 189302-41-8
206749-40-8 206749-41-9 250653-29-3
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of **stabilized** pharmaceuticals contg.
.gamma.-aminobutyric acid derivs.)

RE.CNT 4
RE
(1) Ciba Geigy AG; EP 0376891 A 1990 HCAPLUS
(2) Kigasawa, K; US 4952560 A 1990 HCAPLUS
(3) Nitto Electric Ind Co Ltd; JP 63253022 A 1988 HCAPLUS
(4) Warner Lambert Co; EP 0458751 A 1991 HCAPLUS

L133 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:753060 HCAPLUS
DN 131:356133
TI Solid **compositions** containing .gamma.-aminobutyric acid
derivatives
IN **Aomatsu, Akira**
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9959572	A1	19991125	WO 1999-US10186	19990510	<--
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	AU 9940733	A1	19991206	AU 1999-40733	19990510	<--
	BR 9910494	A	20010109	BR 1999-10494	19990510	<--
	EP 1077691	A1	20010228	EP 1999-924164	19990510	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

	NO 2000005765	A	20001114	NO 2000-5765	20001114	<--
PRAI	JP 1998-133122	A	19980515	<--		
	JP 1998-133112	A	19980515	<--		
	WO 1999-US10186	W	19990510			

OS MARPAT 131:356133

AB The present invention provides a **stabilized** solid **compn**. contg. a 4-amino-3-substituted-butanoic acid deriv. which can be obtained by incorporating a humectant as a **stabilizer**. Bulk powders of **gabapentin** (250 g) were sprayed with 72 g water by means of a fluidized granulator and then dried to give **gabapentin** granular powders A. A second batch of bulk powders of **gabapentin** (250 g) were sprayed with a soln. of 5 g propylene glycol in 67 g water by means of the fluidized granulator and then dried to give **gabapentin** granular powders B. The **gabapentin** granular powders A and B obtained were stored under conditions and then the lactam formed in each of the powders was detd. by HPLC. E.g., **gabapentin** bulk powders stored for 4 wk at 50.degree. and 85% humidity did not show any degrdn.

IT **56-12-2D**, .gamma.-Aminobutyric acid, derivs. **56-40-6**, Glycine, biological studies **56-41-7**, L-Alanine, biological studies **61-90-5**, L-Leucine, biological studies **72-18-4**, L-Valine, biological studies **73-32-5**, L-Isoleucine, biological studies **302-72-7**, Alanine **319-78-8**, D-IsoLeucine **328-38-1**, D-Leucine **328-39-2**, Leucine **338-69-2**, D-Alanine **443-79-8**, Isoleucine **516-06-3**, Valine **640-68-6**, D-Valine **1134-47-0**, **Baclofen** **30200-05-6** **60142-96-3**, **Gabapentin** **148553-50-8**, **Pregabalin** **206749-40-8** **206749-41-9** **250653-29-3**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses) (solid **compns**. contg. .gamma.-aminobutyric acid derivs. and humectants)

RE.CNT 4

RE

(1) Goedecke Ag; DE 3928183 A 1991 HCAPLUS
(2) Kazuo, K; US 4952560 A 1990 HCAPLUS
(3) Nitto Electric Ind Co Ltd; JP 63253022 A 1988 HCAPLUS
(4) Warner Lambert Co; EP 0458751 A 1991 HCAPLUS

L133 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:464180 HCAPLUS

DN 131:111440

TI Methods using agents **simultaneously** acting as NMDA-type glutamate receptor antagonists and GABA-A receptor **agonists** for treating tardive dyskinesia and other movement disorders

IN Fogel, Barry S.

PA Synchroneuron, LLC, USA

SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9936064	A2	19990722	WO 1999-US144	19990113	<--
	WO 9936064	A3	19991202			
	W: AU, CA, CH, CN, JP, MX, NZ					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5952389	A	19990914	US 1998-6641	19980113	<--
	US 6057373	A	20000502	US 1999-224829	19990104	<--
	AU 9921041	A1	19990802	AU 1999-21041	19990113	<--
	EP 1047436	A2	20001102	EP 1999-901314	19990113	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,					

IE, FI
WO 2000028999 A2 20000525 WO 1999-US27343 19991118
WO 2000028999 A3 20000720
W: AU, CA, CH, CN, JP, MX, NZ
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1998-6641 A 19980113 <--
US 1998-193892 A 19981118
US 1999-224829 A 19990104
US 1997-861801 A2 19970522 <--
WO 1999-US144 W 19990113
AB The invention describes treatments for movement disorders, including tardive dyskinesia and tardive dystonia, tic disorders, Tourette's syndrome, blepharospasm, and other focal dystonias. The treatments use agents that **simultaneously** act as NMDA-type glutamate receptor antagonists. Addnl., the treatments of the invention use agents that **simultaneously** act as NMDA-type glutamate receptor antagonists and GABA-A receptor agonists. Preferably, these two activities are characteristic of a single agent, e.g. acamprosate. Alternatively, sep. agents having these activities can be **combined** and administered **together**. The invention also provides a third agent that can be used in **combination** with a treatment for movement disorders, that acts as a non-competitive NMDA-receptor blocking agent or ion channel blocker that augments the effect of the primary treatment. A particularly preferred ion channel blocking agent is magnesium. Alternatively, magnesium can be administered alone for prevention and treatment of movement disorders.
IT **56-12-2**, GABA, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(basal ganglia deficiency; agents **simultaneously** acting as NMDA-type glutamate receptor antagonists and GABA-A receptor agonists for treatment of movement disorders)
IT **6384-92-5**, NMDA
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(excitotoxicity; agents **simultaneously** acting as NMDA-type glutamate receptor antagonists and GABA-A receptor agonists for treatment of movement disorders)

L133 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:219944 HCAPLUS
DN 130:242159
TI **topical** cosmetic or pharmaceutical **compositions** **comprising** an anti-stinging effective amount of an amino acid
IN Muizzuddin, Neelam; Marenus, Kenneth D.; Rein, Glen; Matsui, Mary Steidl
PA E-L Management Corp., USA
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9913819	A2	19990325	WO 1998-US19720	19980921 <--
WO 9913819	A3	19990603		
W: AU, CA, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5958976	A	19990928	US 1997-933571	19970919 <--
AU 9894984	A1	19990405	AU 1998-94984	19980921 <--
EP 957887	A2	19991124	EP 1998-948404	19980921 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001505590	T2	20010424	JP 1999-518281	19980921 <--
PRAI US 1997-933571	A	19970919 <--		
WO 1998-US19720	W	19980921		

AB Topical cosmetic or pharmaceutical **compns. comprising**

an anti-stinging effective amt. of an amino acid selected from the group consisting of an amino butyric acid, glutamine, glycine, and derivs. thereof, or **mixts.** thereof, as well as methods of reducing or preventing stinging using such **compns.** An oil-in-water emulsion contained stearic acid 2.40, glyceryl monostearate 2.20,butyl paraben 0.10, mineral oil/lanolin alc. 9.55, petrolatum/lanolin alc. 2.00, sesame oil 4.30, Pr paraben 0.10, water 72.83, triethanolamine 0.82, Me paraben 0.30, trisodium EDTA 0.10, propylene glycol 4.30, glycine 1.00%. The efficacy of the **compn.** in treatment of lactic acid stinging in volunteers was studied.

IT **56-12-2**, .gamma.-Amino butyric acid, biological studies **56-40-6**, Glycine, biological studies **56-85-9**, Glutamine, biological studies
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(topical cosmetic or pharmaceutical **compns.** **comprising** anti-stinging effective amt. of amino acid)

L133 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:542693 HCAPLUS
DN 129:180125
TI Oral drug delivery **compositions comprising** **modified** amino acids and bioactive peptides
IN Sarubbi, Donald J.; Leone-Bay, Andrea; Paton, Duncan R.
PA Emisphere Technologies, Inc., USA
SO U.S., 18 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 28

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5792451	A	19980811	US 1994-205511	19940302	<--
	CA 2160693	AA	19941027	CA 1994-2160693	19940422	<--
	JP 08509474	T2	19961008	JP 1994-523595	19940422	<--
	EP 1025840	A2	20000809	EP 2000-103527	19940422	<--
	EP 1025840	A3	20000830			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
	EP 1077070	A2	20010221	EP 2000-118505	19940422	<--
	EP 1077070	A3	20010523			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
	US 5643957	A	19970701	US 1994-335148	19941025	<--
	US 5714167	A	19980203	US 1994-328932	19941025	<--
	US 5958457	A	19990928	US 1995-438644	19950510	<--
	US 5766633	A	19980616	US 1995-537888	19951023	<--
	US 6099856	A	20000808	US 1996-763183	19961210	<--
	US 5955503	A	19990921	US 1997-795833	19970206	<--
	US 6100298	A	20000808	US 1997-795837	19970206	<--
	US 6221367	B1	20010424	US 1997-939939	19970929	<--
	US 6071538	A	20000606	US 1997-940056	19970930	<--
	US 6245359	B1	20010612	US 1997-941616	19970930	<--
	US 2001003001	A1	20010607	US 2000-730156	20001205	<--
PRAI	US 1992-898909	B2	19920615	<--		
	US 1992-920346	A2	19920727	<--		
	US 1993-51019	A	19930422	<--		
	US 1993-59019	A2	19930422	<--		
	US 1993-76803	A2	19930614	<--		
	US 1993-143571	B2	19931026	<--		
	US 1993-168776	A2	19931216	<--		
	US 1994-205511	A	19940302	<--		
	EP 1994-916578	A3	19940422	<--		
	US 1994-231622	A2	19940422	<--		
	US 1994-231623	A2	19940422	<--		
	WO 1994-US4560	W	19940422	<--		
	US 1994-315200	A2	19940929	<--		
	US 1994-316404	A2	19940930	<--		

US 1994-328932 A2 19941025 <--
US 1994-335147 B2 19941025 <--
US 1994-335148 A3 19941025 <--
US 1996-17902 P 19960329 <--
US 1996-763183 A2 19961210 <--
US 1997-795837 A1 19970206 <--
US 1997-820694 A2 19970318 <--
US 1997-920346 A2 19970827 <--
US 1999-346970 A1 19990702

AB The present invention relates to an oral drug delivery system, and in particular to modified amino acid derivs. for use as a delivery system of sensitive agents such as bioactive peptides. The modified amino acid derivs. can form non-covalent **mixts.** with active biol. agents and in an alternate embodiment can releasably carry active agents. These **mixts.** are suitable for oral administration of biol. active agents to mammals. Methods for the prepn. of such amino acids are also disclosed.

IT **56-87-1**, Lysine, biological studies **60-18-4**, Tyrosine, biological studies **61-90-5**, Leucine, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(oral drug delivery **compns. comprising** modified amino acids and bioactive peptides)

IT **51-35-4**, Hydroxyproline **52-90-4**, Cysteine, biological studies **56-12-2**, Gaba, biological studies **56-40-6**, Glycine, biological studies **56-41-7**, Alanine, biological studies **56-45-1**, Serine, biological studies **56-84-8**, Aspartic acid, biological studies **56-85-9**, Glutamine, biological studies **56-89-3**, Cystine, biological studies **60-32-2**, .epsilon.-Aminocaproic acid **62-57-7**, .alpha.-Aminoisobutyric acid **63-68-3**, Methionine, biological studies **63-91-2**, Phenylalanine, biological studies **70-26-8**, Ornithine **70-47-3**, Asparagine, biological studies **71-00-1**, Histidine, biological studies **72-18-4**, Valine, biological studies **72-19-5**, Threonine, biological studies **73-22-3**, Tryptophan, biological studies **73-32-5**, Isoleucine, biological studies **74-79-3**, Arginine, biological studies **107-95-9**, .beta.-Alanine **147-85-3**, Proline, biological studies **327-57-1**, Norleucine **372-75-8**, Citrulline **407-41-0 2835-06-5 2835-81-6**, .alpha.-Aminobutyric acid **6600-40-4**, Norvaline
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(oral drug delivery **compns. comprising** modified amino acids and bioactive peptides)

IT **2577-90-4**, Phenylalanine methyl ester
RL: RCT (Reactant)
(oral drug delivery **compns. comprising** modified amino acids and bioactive peptides)

L133 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:323132 HCAPLUS
DN 129:23447
TI A method for treating tension-type headache
IN Olesen, Jes; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
PA Olesen, Jes, Den.; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819674	A2	19980514	WO 1997-DK502	19971104 <--

W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, ES, FI, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9748632 A1 19980529 AU 1997-48632 19971104 <--
EP 1011656 A2 20000628 EP 1997-911150 19971104 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI DK 1996-1243 A 19961105 <--
WO 1997-DK502 W 19971104 <--

AB Tension-type headache is treated by interacting with neuronal transmission in relation to pain in connection with headache in a way which prevents or decreases sensitization of second order nociceptive neurons. In particular, treatment is performed by administration of an effective amt. of a substance which prevents or decreases central sensitization. Important examples of such substances are substances which interact with glutamate neurotransmission, such as glutamate receptor antagonists. Other examples are e.g. substances which interact with nitric oxide, such as nitric oxide synthase (NOS) inhibitors. According to a broader aspect of the invention, tension-type headache is treated by administration of substances which are effective in preventing or decreasing pain in connection with tension-type headache. An addnl. aspect of the invention relates to treatment of tension-type headache by administration of substances which substantially inhibit the activity of NOS. Evidence for central sensitization in chronic myofascial pain, as well as mechanisms of spontaneous tension-type headaches, are also described. **Gabapentin** and dextromethorphen had a prophylactic effect on chronic tension-type headaches.

IT **56-86-0**, L-Glutamic acid, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(glutamate prodn. and release and action; tension-type headache treatment)

IT **56-12-2**, GABA, biological studies **56-40-6**, Glycine, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(prodn. and release and action; tension-type headache treatment)

IT **56-12-2D**, .gamma.-Aminobutyric acid, derivs. **56-40-6D**, Glycine, derivs. **74-79-3D**, L-Arginine, derivs. **372-75-8D**, Citrulline, derivs. **2149-70-4 2149-70-4D**, derivs. **2835-06-5D**, derivs. **17035-90-4 17035-90-4D**, derivs. **22059-21-8 22059-21-8D**, derivs. **50903-99-6**, L-NAME **50903-99-6D**, L-NAME, derivs. **60142-96-3**, **Gabapentin 60142-96-3D**, **Gabapentin**, derivs.
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tension-type headache treatment)

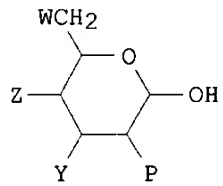
L133 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:483546 HCAPLUS
DN 125:143306
TI Preparation of mono- and dicarboxylic acid amides with amino acids or glycosamines as selectively active cannabinoid peripheral receptor **agonists**
IN Della Valle, Francesco; Leon, Alberta; Marcolongo, Gabriele; Lorenzi, Silvana
PA Lifegroup S.P.A., Italy
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9618600	A1	19960620	WO 1995-EP4926	19951213 <--
	W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2207804	AA	19960620	CA 1995-2207804	19951213 <--
	AU 9643441	A1	19960703	AU 1996-43441	19951213 <--
	EP 799188	A2	19971008	EP 1995-942141	19951213 <--
	EP 799188	B1	19990915		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 11501615	T2	19990209	JP 1995-518264	19951213 <--
	AT 184591	E	19991015	AT 1995-942141	19951213 <--
PRAI	IT 1994-MI2513		19941214 <--		
	WO 1995-EP4926		19951213 <--		

OS MARPAT 125:143306
GI

Q =



AB Title carboxylic acid amides R1CONR1R2 [R1 = linear or branched C9-13 alkyl, optionally contg. one double bond, optionally contg. one or more OH groups, R4CONR5R6, R4CO2R7; R4 = linear or branched C8-22 alkyl, optionally contg. one double bond, optionally substituted with one or more linear or branched C1-8 alkyl groups and/or one or more OH groups; NR2, NR5 = independently optically active or nonactive .alpha.-amino acid contg. aliph. or arylaliph. side chain optionally substituted with OH, OPO3H2, OP(O)(OH)OCH2CH(OH)CH2OH, SH, SMe; a .beta.- or an optionally methylated or ethylated .gamma.-amino acid contg. and aliph. or arylalphatic side chain; or a glycosamine residue Q with one of the groups P, W, Y, Z being N(R3)COR1 and the others being independently H, OH; R3, R6 = independently H, Me; R7 = H, linear or branched C1-20 alkyl], and pharmaceutical **compns**. contg. them for modulation of cannabinoid peripheral receptors are described. Thus, Me(CH2)14CO-L-Ser-OH, prepd. in 89% yield via acylation of L-Ser with palmitoyl chloride in aq. K2CO3, showed 100% displacement of [3H]-WIN 55,212-2 in a cannabinoid receptor membrane assay.

IT **51-35-4**, 4-Hydroxy-L-proline **52-90-4**, L-Cysteine, reactions **56-12-2**, .gamma.-Aminobutyric acid, reactions **56-40-6**, Glycine, reactions **56-45-1**, L-Serine, reactions **107-95-9**, .beta.-Alanine **5680-79-5**, Glycine methyl ester hydrochloride **5680-80-8**, L-Serine methyl ester hydrochloride
RL: RCT (Reactant)
(prepn. of mono- and bicarboxylic acid amides with amino acids or glycosamines as selectively active cannabinoid peripheral receptor agonists)

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FILE 'WPIX' ENTERED AT 12:57:53 ON 12 AUG 2001

FILE LAST UPDATED: 09 AUG 2001 <20010809/UP>
MOST RECENT DERWENT UPDATE 200144 <200144/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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SEE http://www.derwent.com/covcodes.html <<<

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L157 ANSWER 1 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-388393 [41] WPIX
CR 1992-216971 [26]; 1993-386441 [48]; 1996-464187 [46]; 1997-144377 [13];
1997-177956 [16]; 1998-040695 [04]; 1998-129310 [12]; 1999-119283 [10];
2000-194861 [17]; 2000-655473 [54]; 2001-040317 [64]
DNC C2001-118436
TI Treatment of e.g. seizure disorders, Huntington's disease, Parkinson's disease, cerebral ischemia, spasticity, depression and psychosis by administering **4-amino-3-**(2-methylpropyl) **butanoic** acid.
DC B05
IN ANDRUSZKIEWICZ, R; SILVERMAN, R B
PA (NOUN) UNIV NORTHWESTERN
CYC 1
PI US 6197819 B1 20010306 (200141)* 16p A61K031-195 <--
ADT US 6197819 B1 CIP of US 1990-618692 19901127, CIP of US 1992-886080 19920520, Cont of US 1993-64285 19930518, US 1995-420905 19950411
PRAI US 1993-64285 19930518; US 1990-618692 19901127; US 1992-886080 19920520; US 1995-420905 19950411
IC ICM **A61K031-195**
AB US 6197819 B UPAB: 20010724
NOVELTY - **4-amino-3-**(2-methylpropyl) **butanoic** acid (Ia) and its salts are new.
ACTIVITY - Anticonvulsant; antidepressant; anxiolytic; neuroprotective; cerebroprotective; neuroleptic.
4-amino-3-(2-methylpropyl) **butanoic** acid (Ia) had an ED50 for the **gabapentin** receptor of 0.044 micro M.
MECHANISM OF ACTION - Increases brain neuronal GABA.
USE - For treatment of seizure disorders, Huntington's disease, Parkinson's disease, cerebral ischemia, spasticity, depression, anxiety and psychosis in mammals.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B10-B02J; B14-F02D1; B14-J01A1; B14-J01A3; B14-J01A4; B14-J01B3; B14-J01B4; B14-J05A; B14-J05D; B14-J07
TECH UPTX: 20010724
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) are prepared by reduction of a corresponding azide e.g. an azide of formula (II) is reduced to give (Ia).

L157 ANSWER 2 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-040317 [05] WPIX
CR 1992-216971 [26]; 1993-386441 [48]; 1996-464187 [46]; 1997-144377 [13];

1997-177956 [16]; 1998-040695 [04]; 1998-129310 [12]; 1999-119283 [10]; 2000-194861 [17]; 2000-655473 [54]; 2001-388393 [20]
DNC C2001-011567
TI New method of treating seizure disorders and other CNS disorders.
DC B05
IN ANDRUSZKIEWICZ, R; SILVERMAN, R B; YUEN, P
PA (NOUN) UNIV NORTHWESTERN; (WARN) WARNER LAMBERT CO
CYC 1
PI US 6140366 A 20001031 (200105)* 14p A61K031-195 <--
ADT US 6140366 A CIP of US 1990-618692 19901127, CIP of US 1992-886080 19920520, Cont of US 1993-64285 19930518, Div ex US 1995-420905 19950411, Div ex US 1997-899918 19970724, US 1999-244306 19990204
PRAI US 1993-64285 19930518; US 1990-618692 19901127; US 1992-886080 19920520; US 1995-420905 19950411; US 1997-899918 19970724; US 1999-244306 19990204
IC ICM **A61K031-195**
AB US 6140366 A UPAB: 20010724
NOVELTY - Method of treating a patient with cerebral ischemia comprising administration of 1-300 mg/kg of (R-(-)) or S-(+) **4-amino-3-**(2-methylpropyl)**butanoic** acid, is new.
ACTIVITY - Cerebroprotective; antiparkinsonian; anticonvulsant; nootropic; antidepressant; anxiolytic; antipsychotic; vasotropic; .
MECHANISM OF ACTION - GAD activator.
USE - The method is useful in the treatment of cerebral ischemia (claimed), but could also be useful in the treatment of CNS disorders such as epilepsy, Huntington's Chorea, Parkinson's disease, tardive dyskinesia and spasticity, and possibly as antidepressant, anxiolytic and antipsychotic treatment.
ADVANTAGE - The compounds activate GAD in vitro and have a dose-dependent protective effect on seizure in vivo. In assays, it was found that the S-(+)enantiomer of **4-amino-3-**(2-methylpropyl)**butanoic** acid (IBG) potently displaced tritiated **gabapentin** from a novel high-affinity site in rat brain membrane fractions (IC50 of 0.044 mu M, cf. 0.86, 0.10 and 0.14 mu M for (R)-IBG, (plus or minus)-IBG and **gabapentin** respectively). The S-(+)-enantiomer was responsible for all blockade of maximal electroshock seizures in mice and rats.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B10-B02J; B14-J01A1; B14-J01A3; B14-J01B3; B14-J01B4

L157 ANSWER 3 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-105566 [09] WPIX
DNC C2000-031623
TI New composition containing butanoic acid derivatives as tablets or granules.
DC B05
IN **AOMATSU, A**
PA (WARN) WARNER LAMBERT CO
CYC 78
PI WO 9959572 A1 19991125 (200009)* EN 99p A61K031-195 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZA
AU 9940733 A 19991206 (200019) A61K031-195 <--
JP 2000034227 A 20000202 (200021) 34p A61K031-195 <--
BR 9910494 A 20010109 (200106) A61K031-195 <--
NO 2000005765 A 20001114 (200113) A61K031-195 <--
EP 1077691 A1 20010228 (200118) EN A61K031-195 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 9959572 A1 WO 1999-US10186 19990510; AU 9940733 A AU 1999-40733 19990510; JP 2000034227 A JP 1999-133769 19990514; BR 9910494 A BR

1999-10494 19990510, WO 1999-US10186 19990510; NO 2000005765 A WO 1999-US10186 19990510, NO 2000-5765 20001114; EP 1077691 A1 EP 1999-924164 19990510, WO 1999-US10186 19990510

FDT AU 9940733 A Based on WO 9959572; BR 9910494 A Based on WO 9959572; EP 1077691 A1 Based on WO 9959572

PRAI JP 1998-133112 19980515

IC ICM **A61K031-195**
ICS A61K009-14; A61K009-16; A61K009-48; A61K031-00; A61K047-10; A61K047-14; A61K047-18

ICA C07C229-28

AB WO 9959572 A UPAB: 20010110
NOVELTY - A sterilized solid composition containing **4-amino-3**-substituted-**butanoic** acid derivative (I), a humectant and an auxiliary agent if needed, is new.
DETAILED DESCRIPTION - A sterilized solid composition containing **4-amino-3**-substituted-**butanoic** acid derivative of formula (I), a humectant and an auxiliary agent if needed, is new.
R1 = hydrogen atom, hydroxyl, methyl or an ethyl group;
R2 = monovalent group selected from mono- or di-substituted 3-8C alkyl or 3-8C alkylene, mono-, di- or tri-substituted 3-8C cycloalkyl, condensed ring group formed by ortho-fusion of a mono-, di- or tri-substituted phenyl ring with 4-8C or 5-8C cycloalkyl, alkyl 3-8C cycloalkyl linked to 1-4C alkylene (optionally interrupted with -O-, -S-, -SS or mono-, di- or tri-substituted 5-8C cycloalkyl where (-CH2) is replaced by -O-, -NH-, -S-, -SO- or -S(O)2, 5-8C cycloalkenyl or cycloalkanedienyl group where (-CH2) is mono- or di-substituted, alkyl, 5-8C cycloalkyl linked to 1-4C alkylene (optionally mono-, di- or tri-substituted (-CH2) replaced by -O-, -NH-, -S-, -SO- or -S(O)2, optionally mono-, di- or tri- substituted phenyl or naphthyl), alkylphenyl group (optionally mono-, di- or tri- substituted and linked to 1-4C alkylene);
R1 and R2 together with the carbon atom to which they are attached, may form a divalent group with mono-, di-, tri- or tetra-substituted 5-8C cycloalkylidene, condensed group formed by ortho-fusion of mono-, di-, tri- or tetra-substituted phenyl ring with 4-8C cycloalkylidene.
An INDEPENDENT CLAIM is also included for the preparation of a solid composition containing the **4-amino-3**-substituted **butanoic** acid derivative (I) as defined above, a humectant and an auxiliary agent.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - A stabilized solid composition in the form of tablets, powders, granules or capsules (claimed).
ADVANTAGE - Lactam formation during formulation and storage which leads to degradation of the product is prevented by blocking evaporation and movement of residual water by addition of the humectant. The formulation showed increased dissolution and high stability (disclosed).
Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B07-H; B10-A04; B10-A07; B10-B01; B10-B02B; B10-E04C; B12-M11; B14-C01; B14-J01; B14-J07

TECH UPTX: 20000218
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Humectant: 0.01-25% of ethylene glycol, propylene glycol, butylene glycol, sorbitol, glycerol and/or aliphatic acid ester, preferably sorbitol is used as the humectant. 0.1-50% humectant is used for film coated tablets.
Preferred Preparation: Specific amount of (I) is taken and fluidised by fluidised granulation method where a stabilizer (humectant) is sprayed into the powders. The stabilizer is added as a solution, dissolved in water or organic solvent, whereby a small amount is sufficient for uniformly adhering into the powder surface of (I). (I) is combined if necessary with an auxiliary agent, neutral amino acid, binders and sweetening agents. The granules are compressed to form tablets and surface coated if necessary.

Preferred Amino Acid: L-leucine, L-isoleucine, L-valine, L-alanine, D-leucine, D-isoleucine, D-valine, D-alanine, DL-leucine, DL-isoleucine, DL-valine, DL-alanine and/or glycine is used as the amino acid in the composition.

L157 ANSWER 4 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-086571 [07] WPIX
DNC C2000-024063
TI Stabilized pharmaceutical composition containing **4-amino-3**-substituted **butanoic** acid derivative, used for treating cerebral diseases and neurodegenerative disorders.
DC B05
IN **AOMATSU, A**
PA (WARN) WARNER LAMBERT CO
CYC 78
PI WO 9959573 A1 19991125 (200007)* EN 114p A61K031-195 <--
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W: AE AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZA
JP 2000034226 A 20000202 (200017) 40p A61K031-195 <--
AU 9940735 A 19991206 (200019) A61K031-195 <--
BR 9910508 A 20010102 (200104) A61K031-195 <--
NO 2000005768 A 20001114 (200109) A61K000-00
EP 1077692 A1 20010228 (200113) EN A61K031-195 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 9959573 A1 WO 1999-US10190 19990510; JP 2000034226 A JP 1999-133773 19990514; AU 9940735 A AU 1999-40735 19990510; BR 9910508 A BR 1999-10508 19990510, WO 1999-US10190 19990510; NO 2000005768 A WO 1999-US10190 19990510, NO 2000-5768 20001114; EP 1077692 A1 EP 1999-924166 19990510, WO 1999-US10190 19990510
FDT AU 9940735 A Based on WO 9959573; BR 9910508 A Based on WO 9959573; EP 1077692 A1 Based on WO 9959573
PRAI JP 1998-133113 19980515
IC ICM A61K000-00; **A61K031-195**
ICS A61K009-16; A61K009-20; A61K047-16; A61K047-18; **A61P025-00**; **A61P025-28**
ICA A61K009-08; A61K009-14
AB WO 9959573 A UPAB: 20000209
NOVELTY - Stabilized pharmaceutical composition contains a **4-amino-3**-substituted **butanoic** acid derivative (I) and an alpha -**amino** acid.
DETAILED DESCRIPTION - Pharmaceutical composition contains a **4-amino-3**-substituted **butanoic** acid derivative (I), an alpha -**amino** acid and optionally an auxiliary agent.
R1 = H, OH, methyl or ethyl;
R2 = 3-8C alkyl (optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carbalkoxy), 3-8C alkylene, condensed ring formed by ortho-fusion of phenyl (optionally substituted by 1-3 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, carboxy or carbalkoxy) with 4-8C cycloalkyl, 5-8C cycloalkenyl or 5-8C cycloalkanedienyl, alkyl 3-8C cycloalkyl linked through cycloalkyl to 1-4C alkylene optionally interrupted by O, S or SS (with cycloalkyl optionally substituted by 1-3 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carboalkoxy), 5-8C cycloalkyl with one CH2 replaced by O, NH, S, SO or SO2 (with 1 or 2 unsubstituted CH2 optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carboalkoxy), 5-8C cycloalkenyl or cycloalkanedienyl with 1 CH2 replaced by O, NH, N, S, SO or SO2 (with 1 or 2 unsubstituted CH2 optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carboalkoxy), a condensed ring formed by ortho fusion of phenyl with 5-8C cycloalkyl with 1 CH2 replaced by O, NH, S, SO or SO2 (with phenyl optionally substituted by 1 or 2 halo, CF3, OH, alkyl,

alkoxy, alkylthio, NH2, NO2, carboxy or carboalkoxy), a condensed ring formed by ortho fusion of phenyl with 5-8C cycloalkenyl or cycloalkanedienyl with 1 CH2 replaced by O, NH, N, S, SO or SO2 (with phenyl optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, carboxy or carboalkoxy), alkyl 5-8C cycloalkyl with the cycloalkyl linked to 1-4C alkylene optionally interrupted by O, S or SS and 1 CH2 replaced by O, NH, S, SO or SO2 (with 1 or 2 unsubstituted CH2optionally substituted by 1-3 halo. CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carboalkoxy), phenyl (optionally substituted by methylenedioxy) or phenyl or naphthyl (optionally substituted by 1-3 halo, CF3, OH, alkyl, alkoxy, amino, NO2, carboxy, phenoxy, phenylmethoxy (optionally phenyl substituted by halo, CF3, alkoxy, NH2, NO2, carboxy or carboalkoxy) or 5-8C cycloalkylmethoxy with 1 CH2 optionally replaced by O, NH, S, SO or SO2 (optionally ring substituted by halo, CF3, OH, OH, alkyl, alkoxy, NH2, NO2, carboxy or carboalkoxy) or 5-8C cycloalkenylmethoxy or 5-8C cycloalkanedienylmethoxy both with 1 CH2 optionally replaced by O, NH, N, S, SO or SO2 (optionally substituted by halo, CF3, OH, alkyl, alkoxy, NH2, NO2, oxo, carboxy or carboalkoxy)), 1-4C alkylphenyl, alkoxyphenyl, thiophenyl or SS-phenyl (all phenyl linked to 1-4C alkylene via O, S or SS, optionally interrupted by O, S or SS and optionally substituted by 1-3 halo, CF3, OH, alkyl, alkoxy, NH2, NO2 or carboxy) or oxyphenyl, thiophenyl or SS-phenyl (all optionally substituted by 1-3 halo, CF3, OH, aklyl, alkoxy, NH2, NO2 or carboxy) or diphenylamino or

CR1R2 = 5-8C cycloalkylidene (optionally substituted by 1-4 halo, CF3, OH, alkyl, alkoxy, alkylthio, cycloalkyl, phenyl, NH2, NO2 or carboxy), with 1 CH2 optionally replaced by O, NH, S, SO or SO2 and at least 1 unsubstituted CH2 optionally substituted by 1-4 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, carboxy or carboalkoxy, 5-8C cycloalkenylidene or 5-8C cycloalkanedienylidene (both optionally substituted by 1-4 halo, CF3, OH, alkyl, alkoxy, alkylthio, cycloalkyl, phenyl, NH2, NO2, oxo, carboxy or carboalkoxy), with 1 CH2 optionally replaced by O, NH, S, SO or SO2 and at least 1 unsubstituted CH2 optionally substituted by 1-4 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carboalkoxy or a condensed ring formed by ortho fusion of phenyl with 4-8C cycloalkylidene, 5-8C cycloalkenylidene or cycloalkanedienylidene (all optionally phenyl substituted by 1-4 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, carboxy or carboalkoxy).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - For treating cerebral disorders such as epilepsy, hypokinesia, cranial traumas and for treating neurodegenerative disorders such as Alzheimer's disease, Huntington's chorea or Parkinson's disease and amyotrophic lateral sclerosis. The composition is used for improving cerebral functions in senile patients.

ADVANTAGE - Lactam formation through the intramolecular condensation is prevented by blocking both the **amino** group and carbonyl group of (I) by adding an **butanoic** acid derivative and adding an **amino** acid as a stabilizer so that the composition has good storage stability.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B10-B02; B14-J01A3; B14-J01A4; B14-J07; B14-N16; B14-S01

TECH UPTX: 20000209

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The total amount of alpha-**amino** acid is 0.001-80 moles per mole of (I).

The acidic alpha-**amino** acid is used in the form of the corresponding alkali salt acid amide, alkyl-substituted derivative of acid amide or their alkyl esters.

The basic alpha-**amino** acid is used in the form of the corresponding acid addition salt or monoacylated derivative. The acidic alpha-**amino** acid and basic alpha-**amino** acid are also used in the form of corresponding acidic **amino** acid-basic **amino** acid adduct.

The composition contains **gabapentin, pregabalin,**

baclofen, 3-aminomethyl-4-cyclohexyl-**butanoic** acid, 3-aminomethyl-5-cyclohexyl pentanoic acid, 3-aminomethyl-4-phenyl-**butanoic** acid or 3-aminomethyl-5-phenyl-pentanoic acid.

L157 ANSWER 5 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1984-271746 [44] WPIX
DNC C1984-114961
TI Seizure-controlling compsns. contg. GABA-T inhibitor - with glycine, sarcosine or N,N-di methyl glycine synergist.
DC B05 P33
IN SARHAN, S; SEILER, N
PA (RICH) MERRELL DOW PHARM INC; (LTOR) MERRELL TORAUDE & CIE; (LTOR) MERRELL TORAUDE & CIE
CYC 19
PI GB 2138680 A 19841031 (198444)* 11p
EP 124091 A 19841107 (198445) EN
R: AT BE CH DE FR GB IT LI LU NL SE
AU 8426443 A 19841101 (198451)
JP 59206309 A 19841122 (198502)
DK 8402134 A 19841030 (198505)
PT 78492 A 19841220 (198507)
ZA 8403032 A 19841017 (198508)
US 4540582 A 19850910 (198539)
GB 2138680 B 19860521 (198621)
US 4595697 A 19860617 (198627)#
CA 1228818 A 19871103 (198748)
IL 71650 A 19880731 (198846)
EP 124091 B 19891220 (198951) EN
R: AT BE CH DE FR IT LI LU NL SE
DE 3480764 G 19900125 (199005)
JP 05027606 B 19930421 (199319) 10p A61K031-195 <--
ADT GB 2138680 A GB 1984-10504 19840425; EP 124091 A EP 1984-104705 19840426; JP 59206309 A JP 1984-84236 19840427; ZA 8403032 A ZA 1984-3032 19840424; US 4540582 A US 1984-594079 19840328; GB 2138680 B GB 1984-10504 19840425; US 4595697 A Div ex US 1984-594079 19840328, US 1985-705955 19850227; JP 05027606 B JP 1984-84236 19840427
FDT US 4595697 A Div ex US 4540582; JP 05027606 B Based on JP 59206309
PRAI GB 1983-11804 19830429; US 1985-705955 19850227
REP A3...8740; FR 2437834; GB 2120244; No-SR.Pub; US 3960927
IC A61J031-24; A61K031-19; A61K045-06; C07C101-04
ICM **A61K031-195**
ICS A61J031-24; A61K031-19; A61K031-22; A61K045-06; C07C101-04
AB GB 2138680 A UPAB: 19971113
Compsn. comprises (a) a GABA-T inhibitor (I), (b) glycine, sarcosine or N,N-dimethylglycine, or its 1-8C alkyl ester or pharmaceutically acceptable salt, and (c) a carrier or diluent. Pref. (I) is gamma-vinyl GABA, esp. the (s)-isomer free from (R)-isomer; 4-amino-hepta-5,6-dienoic acid; gamma-acetylenic GABA; aminooxyacetic acid ethanolamine o-sulphate; gabaculine; isogabaculine; or their salts.
USE/ADVANTAGE - For treating both convulsive and non-convulsive seizures associated with e.g. epilepsy, trauma, alcohol withdrawals, drug withdrawal, tetanus, metabolic disease, hyperthermia, drug induction and porphyria. The amino acid (b) gives synergistic effects in seizure control, permitting a reduction in the dosage of (I) or permitting greater control at the same dosage. Dose of (I) may be reduced by a factor of 2-5, so that daily dose is 0.2-2 g. p.o. Amt. of (b) is 2-12 g/day, pref. 3-4 g/day.
Dwg.0/0
FS CPI GMPI
FA AB
MC CPI: B10-A09A; B10-A18; B10-B02J; B12-C09; B12-D04; B12-G01
ABEQ EP 124091 B UPAB: 19930925
A pharmaceutical composition for controlling seizures in a patient in need thereof which comprises: (a) gamma-vinyl GABA, or a pharmaceutically acceptable salt thereof, and (b) glycine, sarcosine, or N,N - dimethylglycine, or a C1-C8 alkyl ester thereof, or a pharmaceutically

acceptable salt thereof, in a synergistically effective ratio, and (c) a pharmaceutically acceptable carrier or diluent.

ABEQ GB 2138680 B UPAB: 19930925
A pharmaceutical composition for controlling seizures in a patient in need thereof which comprises: (a) a GABA-T inhibitor (as hereinbefore defined) (b) glycine, sarcosine, or N,N-dimethylglycine, or a C1-C8 alkyl ester thereof, or a pharmaceutically acceptable salt thereof, and (c) a pharmaceutically acceptable carrier or diluent.

ABEQ US 4540582 A UPAB: 19930925
Pharmaceutical compsn. comprises 4-vinyl-**4-aminobutyric** acid (I) or its nontoxic salts (dosage 0.2-2.0 g/day); glycosine, sarcosine or N,N-dimethylglycine or their nontoxic salts or esters (dosage 2-12 g/day); and the usual carriers and additives. Glycine, sarcosine or N,N-dimethylglycine have a synergistic effect on the neurotransmitter inhibiting action of (I) on the central nervous system.

USE - The prods. are improved therapeutic agents for the treatment of convulsive and non-convulsive seizures, esp. epilepsy, trauma, drug withdrawal, tetanus, etc.

ABEQ US 4595697 A UPAB: 19930925
New method for controlling seizures comprises admin. of a 0.2-2 g/day of gamma-vinylCABA (GVG) or its salts and b 2-12 g/day of 1-8C alkyl ester of glycine, sarcosine, N,N-dimethylglycine or salt. Pref. GVG is S isomer S.G.VG. Dosage unit for controlling seizures is a 50-100 mg of GVG or salts; b 250-500 mg 1-8C alkyl esterof glycine, sarcosine, N.N-dimethylglycine or salt and ca carrier or diluent.

ADVANTAGE - S.GVG (4-amino-hex-5-anoic acid) is selective enzyme-activated irreversible inhibitor of GABAltransaminase (GABA-T) which by blocking catabloism of GABA in cns allows its conc. to rise and so inhibit cns neurotransmission. S.GVG is used at half concn. of S.R.GVG in treatment of seisure disorders, esp. epliepsy. Effect is synergistically increased 2-5 times by glycine etc. are also synergistic with GABA-T inhibitors other than GVG.

ABEQ JP 93027606 B UPAB: 19931113
Compsn. comprises (a) a GABA-T inhibitor (I), (b) glycine, sarcosine or N,N-dimethylglycine, or its 1-8C alkyl ester or pharmaceutically acceptable salt, and (c) a carrier or diluent. Pref. (I) is gamma-vinyl GABA, esp.the (s)-isomer free from (R)-isomer; 4-amino-hepta-5,6-dienoic acid; gamma-acetylenic GABA; aminooxyacetic acid ethanolamine o-sulphate; gabaculine; isogabaculine; or their salts.

USE/ADVANTAGE - For treating both convulsive and non-convulsive seizures associated with e.g. epilepsy, trauma, alcohol withdrawals, drug withdrawal, tetanus, metabolic disease, hyperthermia, drug induction and porphyria. The amino acid (b) gives synergistic effects in siezure control, permitting a reduction in the dosage of (I) or permitting greater control at the same dosage. Dose of (I) may be reduced by a factor of 2-5, so that daily dose is 0.2-2 g. p.o. Amt. of (b) is 2-12 g/day, pref. 3-4 g/day. (J59206309-A)

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